Characterising patterns of tumour invasion in glioblastoma

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Target audience: Clinicians treating patients with glioblastoma and imaging scientists interested in imaging glioma invasion.

Purpose: Glioma is the most common primary brain tumour and it has a tendency to invade along and disrupt white matter tracts. Diffusion tensor imaging (DTI) is sensitive to white matter integrity and in the case of glioma decomposing the diffusion tensor into an isotropic component (p) and an anisotropic component (q) has been used previously to investigate patterns of glioma invasion. Characterisation of different invasive phenotypes in glioma is of interest as it may indicate areas where a tumour is likely to reoccur, and additionally, the extent of invasion correlates with progression free survival[1].

Methods: Diffusion tensor imaging was performed preoperatively for a cohort of 46 patients with high-grade glioma (mean age 54.8 years, range 22-73 years; male = 33, female = 13) at 3T on a Siemens Trio. Regions of interest (ROIs) were drawn around the p and q abnormalities for each tumour by an experienced neurosurgeon using ImageJ. The pattern of invasion was then classified as either minimally (n = 7), locally (n = 14) or diffusely (n = 23) invasive by visual inspection of the relative extent of the two abnormalities according to previously published criteria[2]. The inter-rater reliability of assigning invasive patterns was assessed on a subset of 30 patients using ROIs drawn independently by a second experienced neuroradiologist.
We sought to develop an objective method of defining the different invasive phenotypes by measuring the distance between the edges of the p and q ROIs on a slice by slice basis in two dimensions. The Hausdorff distance between the contours defining the regions of interest was calculated using Matlab. Rather than just report the maximum distance between the ROIs we also calculated the median and the 90th percentile of the distances. Differences between the invasive patterns were explored using ANOVA with the Tukey-Kramer HSD post-hoc test and a significance level of 0.05 (IBM SPSS ver22).

Results: There was agreement on the invasive pattern between the two raters in 90% of cases, giving a kappa statistic of 0.81, suggesting good inter-rater reliability, with a consensus being used in cases of disagreement. Significant differences were observed in the median distances between the edges for tumours that were minimally (2.4 ± 0.4 mm) versus locally (4.3 ± 2.0 mm) invasive (P < 0.05), and between minimally and diffusely (5.9 ± 2.8 mm) invasive tumours (P < 0.01). Similarly, the maximum distance between ROIs was significantly different for the minimally (17 ± 4 mm) compared to locally (30 ± 12 mm) invasive tumours (P < 0.05) and between the minimally and diffusively (36 ± 12 mm) invasive tumours (P < 0.05). The 90th percentile of the Hausdorff distance was significantly different between locally (13 ± 5 mm) and diffusely (17 ± 5 mm) invasive tumours (P < 0.05).

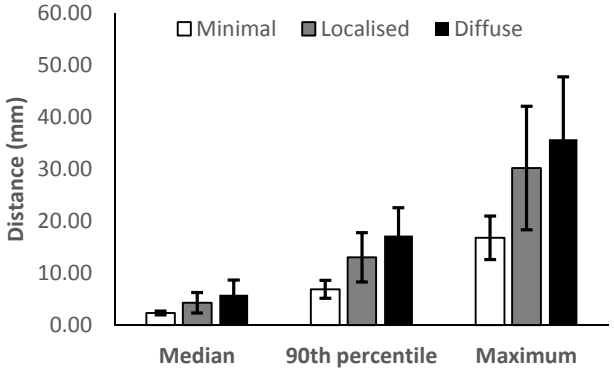

Figure 1. Plot showing comparison between median, 90th percentile and maximum Hausdorff distances between edge pixels of the of the p and q ROIs for different patterns of glioblastoma invasion

Discussion: These results show that the visually assigned invasion patterns are indeed distinct. While locally and diffusely invasive tumours do not have significantly different maximum Hausdorff distances by it is possible to distinguish them using the full distance distribution profile. Further work is underway to develop an automated classifier for assigning different patterns of glioma invasion from DTI data, which may provide prognostic information and identify areas of invasion for more aggressive targeting of therapy.

Conclusion: Patterns of glioma invasion classified visually were shown to be different by an objective analysis.

References:

1. Mohsen LA, Shi V, Jena R, Gillard JH, Price SJ Diffusion tensor invasive phenotypes can predict progression-free survival in glioblastomas. *Br J Neurosurg.* 2013;27:436-441
2. Price SJ, Jena R, Burnet NG, Carpenter TA, Pickard JD, Gillard JH. Predicting patterns of glioma recurrence using diffusion tensor imaging. *Eur. Radio.* 2007;17:1675-1684